

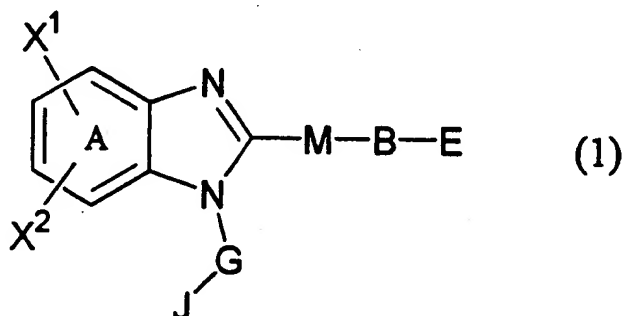
AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

LISTING OF CLAIMS:

1-21. (canceled)

22. (previously presented): A method of inhibiting human chymase activity to treat or prevent a bone/cartilage metabolic disease in human beings, said method comprising administering to a subject an effective amount of a benzimidazole derivative expressed by the



following formula (1) or its pharmaceutically permissible salt,

[in the formula (1), the ring marked with A expresses a benzene ring;

X¹ and X² are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group), -COOR³ (here, R³ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkyl group, a substituted or unsubstituted C₃₋₇ cycloalkyl group, a substituted or unsubstituted C₁₋₆ normal or branched alkoxy group, a substituted or unsubstituted C₁₋₆ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₆ normal or branched

alkylsulfonyl group or a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkylene group or a substituted or unsubstituted C₂₋₆ normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the M, and here R⁴ is a hydrogen atom or a C₁₋₆ normal or branched alkyl group};

E expresses -COOR⁴;

G is a substituted or unsubstituted C₁₋₆ normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R⁴ is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro

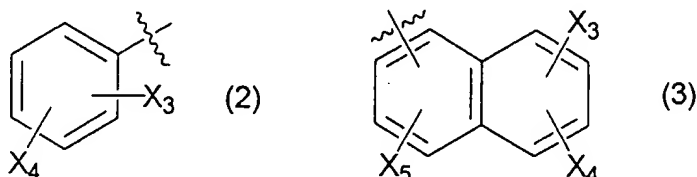
group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C₄₋₁₀ aryl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, -COOR⁷ (here, R⁷ is a hydrogen atom or a C₁₋₄ alkyl group), a C₁₋₆ normal, cyclic or branched alkyl group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched alkylsulfinyl group, a C₁₋₆ acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; and

M is a sulfur atom, a sulfinyl group, or a sulfonyl group].

23. (previously presented): The method set forth in Claim 22 wherein X¹ and X² in the above formula (1) are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a substituted or unsubstituted C₁₋₃ normal or branched alkyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkoxyl group, or a substituted or unsubstituted C₁₋₃ normal or branched alkylthio group.

24. (previously presented): The method set forth in Claim 22 wherein J in formula (1) is a group described in the following formula (2) or (3),



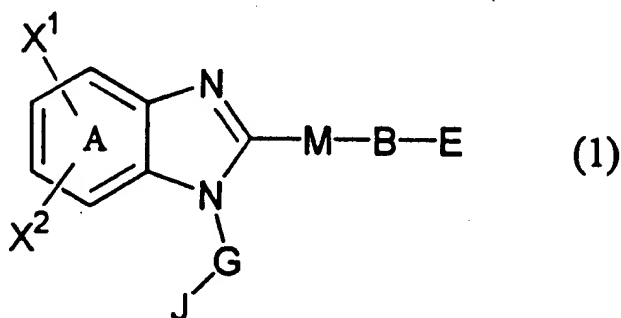
[here, X³, X⁴ and X⁵ are each at the same time or independently a hydrogen atom, a halogen atom, a hydroxyl group, a nitro group, a cyano group, a trihalomethyl group, a trihalomethoxy group, -COOR⁷ (here, R⁷ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₃ normal or branched alkyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkoxyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfonyl group, or a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of X³, X⁴ and X⁵ on the benzene ring or the naphthalene ring].

25. (previously presented): The method set forth in Claim 22 wherein M is a sulfur atom.

26. (previously presented): The method set forth in Claim 22 wherein B is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkylene group.

27. (previously presented): The method set forth in Claim 22 wherein G is -CH₂-, -CH₂CH₂-, -CH₂CO-, -CH₂CH₂O-, -CH₂CONH-, -CO-, -CH₂SO₂-, -CH₂S- or -CH₂CH₂S- (J bonds to the right side of said group).

28. **(previously presented):** The method set forth in Claim 22 wherein E is -COOH.
29. **(currently amended):** A benzimidazole derivative expressed by the following formula (1) or its pharmaceutically permissible salt,



[in the formula (1), the ring marked with A expresses a benzene ring;

X¹ and X² are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group), -COOR³ (here, R³ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkyl group, a substituted or unsubstituted C₃₋₇ cycloalkyl group, a substituted or unsubstituted C₁₋₆ normal or branched alkoxy group, a substituted or unsubstituted C₁₋₆ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfonyl group or a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkylene group or a substituted or unsubstituted C₂₋₆ normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S- or -SO₂-, but this atom or atomic group does not bond directly to the M, and here R⁴ is a hydrogen atom or a C₁₋₆ normal or branched alkyl group};

E expresses -COOR⁴;

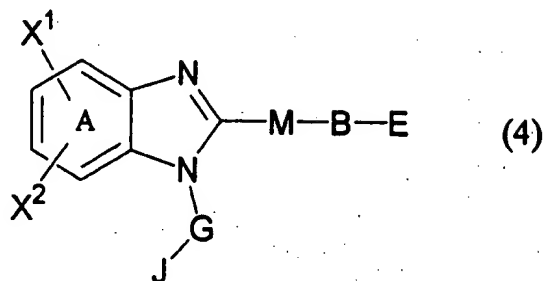
G is a substituted or unsubstituted C₁₋₆ normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R⁴ is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C₄₋₁₀ aryl group, provided that J is not phenyl group, {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a

cyano group, -COOR^7 (here, R^7 is a hydrogen atom or a C_{1-4} alkyl group), a C_{1-6} normal, cyclic or branched alkyl group, a C_{1-6} normal or branched alkoxy group (including the case where adjacent two groups form an acetal bonding), a C_{1-6} normal or branched alkylthio group, a C_{1-6} normal or branched alkylsulfonyl group, a C_{1-6} normal or branched alkylsulfinyl group, a C_{1-6} acyl group, a C_{1-6} normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; and
M is a sulfinyl group, or a sulfonyl group].

30. (previously presented): The benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 wherein X^1 and X^2 in the above formula (1) are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a cyano group, a substituted or unsubstituted C_{1-3} normal or branched alkyl group, a substituted or unsubstituted C_{1-3} normal or branched alkoxy group, or a substituted or unsubstituted C_{1-3} normal or branched alkylthio group.

31. (currently amended): A benzimidazole derivative expressed by the following formula (4) or its pharmaceutically permissible salt,



[in the formula (4), the ring marked with A expresses a benzene ring;

X^1 and X^2 are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, a cyano group, $-\text{CH}_2\text{NH}_2$, $-\text{CH}=\text{NR}^1$, $-\text{CH}=\text{NOR}^1$ or $-\text{CONR}^1\text{R}^2$ (here, R^1 and R^2 are each a hydrogen atom or a C_{1-4} alkyl group), $-\text{COOR}^3$ (here, R^3 is a hydrogen atom or a C_{1-4} alkyl group), a substituted or unsubstituted C_{1-6} normal, cyclic or branched alkyl group, a substituted or unsubstituted C_{3-7} cycloalkyl group, a substituted or unsubstituted C_{1-6} normal or branched alkoxy group, a substituted or unsubstituted C_{1-6} normal or branched alkylthio group, a substituted or unsubstituted C_{1-6} normal or branched alkylsulfonyl group or a substituted or unsubstituted C_{1-6} normal or branched alkylsulfinyl group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)};

B is a substituted or unsubstituted C_{1-6} normal, cyclic or branched alkylene group or a substituted or unsubstituted C_{2-6} normal or branched alkenylene group {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C_{1-6} normal or branched alkoxy group (including the case where adjacent two groups form an

acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s) of the alkylene group or an alkenylene group; between atoms, the alkylene group or alkenylene group optionally contains one or more of -O-, -S- or -SO₂-, but this atom or atomic group does not bond directly to the M, and here R⁴ is a hydrogen atom or a C₁₋₆ normal or branched alkyl group};

E expresses -COOR⁴;

G is a substituted or unsubstituted C₁₋₆ normal or branched alkylene group {between atoms, the alkylene group optionally contains one or more of -O-, -S-, -SO₂- or -NR⁴-, but this atom or atomic group does not bond directly to the nitrogen atom of the imidazole ring (R⁴ is similarly defined as above), and the substituent is a halogen atom, a hydroxyl group, a nitro group, a cyano group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a trihalomethyl group, a trihalomethoxy group, a phenyl group or an oxo group};

J is a substituted or unsubstituted C₄₋₁₀ aryl group, provided that J is not phenyl group, {the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, -COOR⁷ (here, R⁷ is a hydrogen atom or a C₁₋₄ alkyl group), a C₁₋₆ normal, cyclic or branched alkyl group, a C₁₋₆ normal or branched alkoxyl group (including the case where adjacent two groups form an acetal bonding), a C₁₋₆ normal or branched alkylthio group, a C₁₋₆ normal or branched alkylsulfonyl group, a C₁₋₆ normal or branched alkylsulfinyl group, a C₁₋₆

acyl group, a C₁₋₆ normal or branched acylamino group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group, or a phenoxy group optionally substituted with one or more halogen atoms; the substituent may substitute singly or plurally independently at arbitrary position(s) of the aryl group; and the substituent is further optionally substituted with a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a phenyl group, an oxo group or a phenoxy group optionally substituted with a halogen atom}; and

M is a sulfur atom, a sulfinyl group, or sulfonyl group;

provided that when X¹ and X² are each a group other than a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group), J is a substituted naphthalene ring.

32. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X¹ and X² are each a hydrogen atom, a cyano group, -CH₂NH₂, -CH=NR¹, -CH=NOR¹ or -CONR¹R² (here, R¹ and R² are each a hydrogen atom or a C₁₋₄ alkyl group; X¹ and X² are not hydrogen at the same time).

33. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X¹ and X² are each at the same time or independently a hydrogen atom, a halogen atom, a trihalomethyl group, a hydroxyl group, a nitro group, -COOR³ (here, R³ is a hydrogen atom or a C₁₋₄ alkyl group), a substituted or unsubstituted C₁₋₆ normal, cyclic or branched alkyl group, a substituted or unsubstituted C₃₋₇ cycloalkyl, a substituted or unsubstituted C₁₋₆ normal or branched alkoxyl group, a substituted or unsubstituted C₁₋₆ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfonyl group or a substituted or unsubstituted C₁₋₆ normal or branched alkylsulfinyl group

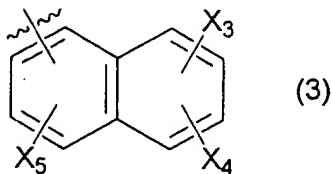
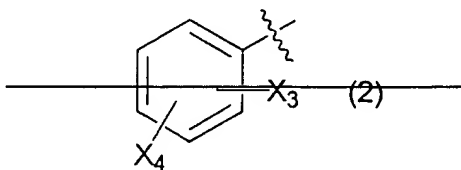
{the substituent permissible to the groups is a halogen atom, a hydroxyl group, a nitro group, a cyano group, an acyl group, a trihalomethyl group, a trihalomethoxy group, a phenyl group, an oxo group or a phenoxy group optionally substituted with one or more halogen atoms, and the substituent may substitute singly or plurally independently at arbitrary position(s)}.

34. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein X^1 and X^2 are each a hydrogen atom or a cyano group (here, X^1 and X^2 can not be hydrogen atoms at the same time).

35. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 31 wherein M is a sulfur atom.

36. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein B is a substituted or unsubstituted C_{1-6} normal, cyclic or branched alkylene group.

37. (currently amended): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein J is a group expressed by the following formula (2) or (3),



[here, X^3 , X^4 and X^5 are each at the same time or independently a hydrogen atom, a halogen atom, a hydroxyl group, a nitro group, a cyano group, a trihalomethyl group, a trihalomethoxy group, $-COOR^7$ (here, R^7 is a hydrogen atom or a C_{1-4} alkyl group), a substituted

or unsubstituted C₁₋₃ normal or branched alkyl group, a substituted or unsubstituted C₁₋₃ normal or branched alkoxy group, a substituted or unsubstituted C₁₋₃ normal or branched alkylthio group, a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfonyl group, or a substituted or unsubstituted C₁₋₃ normal or branched alkylsulfinyl group; there is no limitation regarding the substitution positions of X³, X⁴ and X⁵ on the benzene ring or the naphthalene ring].

38. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein G is -CH₂-, -CH₂CH₂-, -CH₂CO-, -CH₂CH₂O-, -CH₂CONH-, -CO-, -CH₂SO₂-, -CH₂S- or -CH₂CH₂S- (J bonds to the right side of said group).

39. (previously presented): A benzimidazole derivative or its pharmaceutically permissible salt set forth in Claim 29 or 31 wherein E is -COOH.

40. (previously presented): A pharmaceutical composition consisting of a benzimidazole derivative and/or its pharmaceutically permissible salt set forth in any one of Claims 29, 30 or 31, and a pharmaceutically permissible carrier.

41. (previously presented): A method of preventing or treating an inflammatory disease, an allergy disease, a respiratory disease, a cardiovascular disease or a bone/cartilage metabolic disease, said method comprising administering to a subject an effective amount of a benzimidazole derivative or its pharmaceutically permissible salt set forth in any one of Claims 29, 30 or 31.

42. (previously presented): The method set forth in Claim 41 to prevent or treat a disease in human beings.